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EXAMINER	
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1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,051	ST. JOHN ET AL.	
	Examiner	Art Unit	
	FRANK W. LU	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 19-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/18/2008 and 6/10/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-14 and 19-26 in the reply filed on March 29, 2010 is acknowledged.

Information Disclosure Statement

2. Since the examiner cannot locate an International Preliminary Report mailed on March 12, 2009 in this instant case, this report in 1449 form filed on June 10, 2009 has not been considered and has been struck-through.

Specification

3. The disclosure is objected to because of the following informalities: there are a lot of nucleotide sequences having more than 10 nucleotides in Figures 1-3. However, there are no SEQ ID NOs in Figures 1-3 or BRIEF DESCRIPTION OF THE DRAWINGS related to Figures 1-3 of the specification do not describe these nucleotide sequences.

Appropriate correction is required.

Claim Objections

4. Claim 1 or 11 or 14 or 19 or 23 or 24 or 26 is objected to because of the following informality: no period should appear after the label of each step, e.g., "a." should be --a)--.

5. Claim 1 is objected to because of the following informality: (1) "complimentary" in step a) should be "complementary"; and (2) "the high complexity nucleic acid molecules" in step e) should be "the high complexity nucleic acid molecule" in view of step a).

6. Claim 3 is objected to because of the following informality: "temperature of between about 45°C and about 70°C" in line 3 should be "temperature between about 45°C and about 70°C".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-14 and 19-26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 1 is rejected as vague and indefinite because it is unclear that a high complexity nucleic acid molecule in step a) is from high complexity nucleic acid fragments or not. Please clarify.

10. Claim 5 recites the limitation "the streptavidin-coated magnetic beads" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase "streptavidin-coated magnetic beads" in claim 1. Please clarify.

11. Claim 6 is rejected as vague and indefinite. Although claim 6 comprises the additional step of ligating at least one DNA linker to the ends of digested high complexity nucleic acid fragments to form ligated nucleic acid fragments prior to the hybridizing step, since claim 6 is dependent on claim 1 and there are no ligated nucleic acid fragments, it is unclear how ligated nucleic acid fragments in claim 6 is correlated with the method steps of claim 1. Please clarify.

12. Claim 10 recites the limitation "the magnetic beads" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase "magnetic beads" in claim 1. Please clarify.

13. Claim 11 recites the limitation "the isolated high complexity nucleic acid fragment" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase "isolated high complexity nucleic acid fragment" in claim 1. Please clarify.

14. Claim 12 is rejected as vague and indefinite. Although claim 12 comprises the additional step of ligating at least one DNA linker to the ends of digested high complexity nucleic acid fragments to form ligated nucleic acid fragments prior to the hybridizing step, since claim 12 is dependent on claim 11 which is dependent on claim 1 and there are no ligated nucleic acid fragments, it is unclear how ligated nucleic acid fragments in claim 12 is correlated with the method steps of claim 1. Please clarify.

15. Claim 14 recites the limitation "the ligated vector" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no "ligated vector" before "the ligated vector" in claim 14. Please clarify.

16. Claim 14 recites the limitation "the amplified vector" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no "amplified vector" before "the amplified vector" in claim 14. Please clarify.

17. Claim 19 is rejected as vague and indefinite because it is unclear that the nucleic acid molecules in step e) means digested nucleic acid fragments or ligated products comprising at least one DNA linker and digested nucleic acid fragments. Please clarify.

18. Claim 24 recites the limitation "the isolated high complexity nucleic acid fragment" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase "isolated high complexity nucleic acid fragment" in claim 19. Please clarify.

19. Claim 26 recites the limitation "the ligated vector" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no "ligated vector" before "the ligated vector" in claim 26. Please clarify.

20. Claim 26 recites the limitation "the amplified vector" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no "amplified vector" before "the amplified vector" in claim 26. Please clarify.

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Cimino *et al.,* (US Patent No. 5,221,608, published on June 22, 1993).

Regarding claims 1 and 2, Cimino *et al.,* teach a method of isolating a high complexity nucleic acid molecule comprising: a) hybridizing high complexity nucleic acid fragments (ie., the target DNA in a mixture of DNA) to a functionalized nucleic acid probe (i.e., the biotinylated probe) having a sequence complementary to at least a portion of a high complexity nucleic acid molecule to form hybridized nucleic acid fragments; b) complexing the functionalized nucleic acid probe with a capture agent (ie., avidin-agarose); c) immobilizing the capture agent (ie., on

an avidin-agarose column); and, d) eluting (ie., eluting by denaturation) the high complexity nucleic acid molecule (ie., the target DNA) from the functionalized nucleic acid probe (ie., the biotinylated probe) as recited in claim 1 wherein the functionalized nucleic acid probe is a biotinylated nucleic acid probe as recited in claim 2 (see column 43, lines 46-67 and column 44, lines 1-13).

Therefore, Cimino *et al.,* teach all limitations recited in claims 1 and 2.

Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

24. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cimino *et al.,* as applied to claims 1 and 2 above, and further in view of Collins *et al.,* (US Patent No.4,818,680, published on April 4, 1989).

The teachings of Cimino *et al.,* have been summarized previously, *supra.*

Cimino *et al.,* do not disclose that the hybridizing step comprises incubating the high complexity nucleic acid fragments with a biotinylated nucleic acid probe at a temperature between about 45°C and about 70°C for about 1 hour.

Collins *et al.,* teach to perform a hybridization reaction at 65°C for 60 minutes (see Example 6, column 19).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 3 wherein the hybridizing step comprises incubating the high complexity nucleic acid fragments with a biotinylated nucleic acid probe at a temperature between about 45°C and about 70°C for about 1 hour (ie., 65°C for 60 minutes) in view of the prior art of Cimino *et al.,* and Collins *et al.*. One having ordinary skill in the art would have been motivated to do so because Collins *et al.,* have shown to perform a hybridization reaction at 65°C for 60 minutes (see Example 6, column 19) and the simple substitution of one kind of hybridization condition (ie., the hybridization condition taught by Cimino *et al.,*) from another kind of hybridization condition (ie., the hybridization condition taught by Collins *et al.,*) during the process of performing the method recited in claim 1, in the absence of convincing evidence to the contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the hybridization condition taught by Cimino *et al.,* and the hybridization condition taught by Collins *et al.,* are used for the same purpose (ie., a nucleic acid hybridization reaction) and are exchangeable.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

25. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cimino *et al.,* as applied to claims 1 and 2 above, and further in view of Weiner (US Patent No. 5,851,759, published on December 22, 1998).

The teachings of Cimino *et al.,* have been summarized previously, *supra.*

Cimino *et al.,* do not disclose that the capture agent comprises streptavidin-coated magnetic beads as recited in claim 4.

Weiner teaches to elute a non-biotinylated single strand from a double stranded cDNA which has a biotinylated single strand and is bound to a magnetic bead/streptavidin column (see Examples 2 and 3 in columns 9 and 10).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 4 wherein the capture agent comprises streptavidin-coated magnetic beads in view of the prior art of Cimino *et al.,* and Weiner. One having ordinary skill in the art would have been motivated to do so because both avidin and streptavidin bind to biotin (see Cimino *et al.,* column 43, lines 46-67 and

Weiner, column 10, last paragraph) and the simple substitution of one kind of capture agent (ie., the avidin-agarose taught by Cimino *et al.,*) from another kind of capture agent (ie., the magnetic bead/streptavidin taught by Weiner) during the process of performing the method recited in claim 1, in the absence of convincing evidence to the contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the avidin-agarose taught by Cimino *et al.,* and the magnetic bead/streptavidin taught by Weiner are used for the same purpose (ie., separating a biotinylated nucleic acid strand from a non-biotinylated nucleic acid strand) and are exchangeable.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

26. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cimino *et al.,* in view of Weiner as applied to claims 1, 2, and 4 above, and further in view of Deshayes *et al.,* (US Patent No.7,071,300, filed on March 13, 2002).

The teachings of Cimino *et al.,* and Weiner have been summarized previously, *supra.*

Cimino *et al.,* and Weiner do not disclose that the streptavidin-coated magnetic beads comprise a protein-blocking material as recited in claim 5.

Deshayes *et al.,* teach streptavidin-linked magnetic beads which are previously blocked with BSA (see Example 1, column 40, second paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 5 wherein streptavidin-coated magnetic beads comprise a protein-blocking material (ie., BSA) in view of the prior art of Cimino *et al.,* Weiner and Deshayes *et al.*. One having ordinary skill in the art would have been motivated to do so because Deshayes *et al.,* have taught streptavidin-linked magnetic beads which are previously blocked with BSA (see Example 1, column 40, second paragraph) and coating a blocking agent such as BSA onto the streptavidin-coated magnetic beads would reduce non-specific binding or non-specific hybridization, and the simple substitution of one kind of streptavidin-coated magnetic beads (ie., the streptavidin-coated magnetic beads taught by Weiner) from another kind of affinity column (ie., the streptavidin-coated magnetic beads taught by Deshayes *et al.,*) during the process of performing the method recited in claim 4, in the absence of convincing evidence to the contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the streptavidin-coated magnetic beads taught by Weiner and the streptavidin-coated magnetic beads taught by Deshayes *et al.,* are used for the same purpose (ie., binding to a biotinylated target) and are exchangeable.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

27. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cimino *et al.,* as applied to claims 1 and 2 above, and further in view of Sutcliffe *et al.,* (US Patent No. 6,596,484 B1, filed on August 29, 2000).

The teachings of Cimino *et al.,* have been summarized previously, *supra.*

Cimino *et al.,* do not disclose the additional steps of amplifying the isolated high complexity nucleic acid fragment and sequencing the amplified high complexity nucleic acid fragment as recited in claim 11.

Sutcliffe *et al.,* teach amplifying the eluted cDNA in a polymerase chain reaction, cloning the amplified cDNA into a plasmid, producing DNA corresponding to the cloned DNA from the plasmid and sequencing the cloned cDNA (see column 10, lines 1-16).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 11 by further amplifying the isolated high complexity nucleic acid fragment and sequencing the amplified high complexity nucleic acid fragment in view of the prior art of Cimino *et al.,* and Sutcliffe *et al.*. One having ordinary skill in the art would have been motivated to do so because Sutcliffe *et al.,* have taught amplifying the eluted cDNA in a polymerase chain reaction, cloning the amplified cDNA into a plasmid, producing DNA corresponding to the cloned DNA from the plasmid and sequencing the cloned cDNA (see column 10, lines 1-16). One having ordinary skill in the art at

the time the invention was made would have been a reasonable expectation of success to amplify the isolated high complexity nucleic acid fragment and sequence the amplified high complexity nucleic acid fragment in order to make more isolated high complexity nucleic acid fragment and obtain the sequence information of the amplified high complexity nucleic acid fragment.

Conclusion

28. No claim is allowed.

29. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached on (571)272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Frank W Lu /,
Primary Examiner, Art Unit 1634
June 21, 2010